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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/643,589	08/18/2003	Debra D. Pittman	WYTH-P01-002	3988

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EXAMINER	
EMCH, GREGORY S	

ART UNIT	PAPER NUMBER
1649	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/643,589	PITTMAN ET AL.	
	Examiner	Art Unit	
	Gregory S. Emch	1649	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *30 July 2008 and 20 February 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,3-58 and 85-92* is/are pending in the application.

4a) Of the above claim(s) *32-41,45-58 and 85-87* is/are withdrawn from consideration.

5)☒ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,8-31 and 42-44* is/are rejected.

7)☐ Claim(s) *3-7 and 88-92* is/are objected to.

8)☒ Claim(s) *1,3-58 and 85-92* are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *02/20/08*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Response to Amendment

Claims 1, 14, 15, 20, 42, 43, 45, 48, 85 and 87 have been amended, and claims 2 and 59-71 have been canceled as requested in the amendment filed on 30 July 2008. Following the amendment, claims1, 3-58 and 85-92 are pending in the instant application.

Claims 32-41, 45-58 and 85-87 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim.

Claims 1, 3-31, 42-44 and 88-92 are under examination in the instant office action.

Any objection or rejection of record, which is not expressly repeated in this action has been overcome by Applicants' response and withdrawn.

Formal Matters

It is noted that current claim listing submitted 30 July 2008 is still considered non-compliant (see 37 CFR §1.121), e.g. it contains incorrect claim identifiers. However, in the interest of advancing prosecution, the instant office action has been prepared. **Applicants are advised to take notice of the status of the claims as correctly outlined by the Examiner herein (both above and on form PTO-326) and to correct the claim identifiers in the next reply to the instant office action.**

Information Disclosure Statement

A signed and initialed copy of the IDS paper filed on 20 February 2008 is enclosed in this action.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicants are advised of the

obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

The rejection of claims 1, 8-31 and 42-44 under 35 U.S.C. 103(a) as being unpatentable over U.S. Patent No. 5,864,018 to Morser et al. in view of Peppel et al. (J Exp Med. 1991 Dec 1;174(6):1483-9), further in view of U.S. 20020102604 to Milne Edwards et al. and as evidenced by WO 94/10308 to Spriggs et al. is maintained for reasons of record and as set forth below.

The claims are directed to a fusion protein comprising a Receptor for Advanced Glycation End Product Ligand Binding Element (RAGE-LBE) and an immunoglobulin element, wherein the RAGE-LBE comprises at least 118 amino acids and is at least 95% identical to amino acid residues 1 through 118 of SEQ ID NO: 7; further comprising a dimerizing polypeptide (including an amphiphilic polypeptide), a purification polypeptide, a stabilizing polypeptide, or a targeting polypeptide, and associated protein complexes and pharmaceutical compositions that additionally comprise a TNF-α inhibitor.

In the reply filed on 20 February 2008, Applicants assert that Morser et al. disclose fusion proteins comprising RAGE polypeptides and fragments thereof but do not teach or suggest the human RAGE-LBE as recited in claims 1 and 20 or the mouse RAGE-LBE as recited in claims 85 and 87. Applicants assert that none of the other cited references bridge the gap between Morser et al. and the claimed invention.

Applicants assert that even if Morser et al. is combined with the other cited references, the combination still fails to provide any suggestion or motivation for a skilled artisan to modify Morser's RAGE polypeptides to arrive at the claimed RAGE-LBE fusion proteins. Applicants assert that Morser provides no teaching or suggestion that RAGE polypeptides need to be further modified to improve their suitability or efficacy for any application. Applicants assert that the Examiner has indicated that claims 3-7 and 88-92 (directed to specific sequences of RAGE-LBE) are not obvious over the cited references. Applicants assert that amended claims 1 and 20 are essentially drawn to the subject matter of claims 3-7 and 88-92. Thus, Applicants believe amendments to claims 1 and 20 obviate the obviousness rejection.

Applicants' arguments have been fully considered and are not found persuasive. The ‘018 patent to Morser et al. discloses fusion proteins comprising RAGE polypeptides, including a polypeptide that is at least 118 amino acids and is at least 95% identical (i.e. 99.7% identical) to amino acid residues 1 through 118 of SEQ ID NO: 7 (see attached sequence alignment B), and fragments, including but not limited to ligand binding elements (e.g. soluble portions or RAGE) and immunoglobulin-like domains (col.7, line 45; col.8, lines 7-14; col.22, line 26-29), as in the instant claims 1 and 20. Thus, Applicants’ assertion that Morser et al. do not teach or suggest the human RAGE-LBE as recited in claims 1 and 20 is inaccurate. Regarding Applicants’ assertion that involves claims 85-87, Applicants are reminded that claims 85-87 are withdrawn from consideration and are not under examination in the instant office action.

Applicants' assertions that there is no suggestion or motivation to combine the cited references and arrive at the claimed invention is inaccurate. The motivation to combine can be found in the Morser et al. patent and the Peppel et al. reference. Specifically, the Morser et al. patent teaches that inventive compositions can comprise soluble RAGE polypeptides, i.e. fragments of RAGE that lack the transmembrane or cytoplasmic domains, and methods of using these compositions in screening, therapeutic and diagnostic applications, e.g. as blocking agents to inhibit or otherwise reduce the AGE/RAGE (ligand/receptor) interaction (col.4, line 58 - col.5, line 2). Furthermore, the Peppel et al. reference teaches that truncated receptor molecules, i.e. fragments that lack the transmembrane or cytoplasmic domains, are capable of interacting with TNF and can act as antagonists of TNF and as reagents to be used in defining the interaction between TNF and its receptor (ligand/receptor). The Peppel et al. reference teaches the desirability (e.g. increased stability and ease of purification) of engineering a chimeric protein in which the extracellular domain of the receptor, which normally engages the ligand, is covalently linked to IgG immunoglobulin domains (p.1483). Therefore, as evidenced by the prior art (i.e. the Morser et al. patent), the skilled artisan would have known that developing compositions comprising fusion proteins comprising RAGE ligand binding fragments would be desirable. Furthermore, it would have been reasonable to predict that a fusion protein model taught by the Peppel et al. reference, i.e. an extracellular or soluble portion of a receptor linked to an immunoglobulin element, could be successfully used as the fusion protein model for the Morser et al. compositions comprising RAGE-LBE fusion proteins. Thus, it would have

been obvious to the person of ordinary skill in the art at the time the invention was made to improve Morser et al.'s fusion proteins as disclosed by Peppel et al. to yield predictable results. This is because the artisan has good reason to pursue the known options within his or her technical grasp to obtain predictable results. Such would amount to a substitution of one known equivalent element for another to yield predictable results. This is because a fusion protein comprising an extracellular or soluble portion of a TNF receptor as taught by Peppel et al. is analogous to a fusion protein comprising an extracellular or soluble portion of the RAGE receptor as taught by Morser et al.

Regarding Applicants' assertion that Morser provides no teaching or suggestion that RAGE polypeptides need to be further modified to improve their suitability or efficacy for any application, it is not necessary that the reference teach such. The Peppel et al. reference provides a suggestion and motivation to modify the Morser et al. fusion proteins to improve their stability and ease of purification. Applicants are reminded that only a reason, suggestion or motivation need appear in the cited prior art in order to combine references under 35 U.S.C. 103. *Pro Mold Tool Col. v. Great Lakes Plastics, Inc.,* 75 F.3d 1568, 1573, 37 USPQ2d 1626, 1629 (Fed. Cir. 1996). Moreover, the motivation to combine can arise from the expectation that the prior art elements will perform their expected functions to achieve their expected results when combined for their common known purpose (MPEP §2144.07).

Applicants' assertions that amended claims 1 and 20 are essentially drawn to the subject matter of claims 3-7 and 88-92, and thus, that the amendments to claims 1 and

20 obviate the obviousness rejection is inaccurate. Although dependent claims 3-7 and 88-92, are close in scope to the subject matter of claims 1 and 20, they are not drawn to the same subject matter. Claims 1 and 20 only require that the RAGE-LBE comprises at least 118 amino acids and is at least 95% identical to amino acid residues 1 through 118 of SEQ ID NO: 7. This is distinguished from the dependent claims, which require that: the RAGE-LBE comprises amino acid residues 1 through 344 of SEQ ID NO: 7 (claims 3 and 88), the RAGE-LBE comprises amino acid residues 1 through 330 of SEQ ID NO: 7 (claims 4 and 89), the RAGE-LBE comprises amino acid residues 1 through 321 of SEQ ID NO: 7 (claims 5 and 90), the RAGE-LBE comprises amino acid residues 1 through 230 of SEQ ID NO: 7 (claims 6 and 91), and the RAGE-LBE comprises amino acid residues 1 through 118 of SEQ ID NO: 7 (claims 7 and 92). Thus, the mismatch at residue 110 shown in Sequence Alignment B disqualifies the Morser et al. patent as prior art for claims 3-7 and 88-92, because these claims require no mismatch at residue 110. However, this mismatch at residue 110 does not disqualify the Morser et al. patent as prior art for claims 1 and 20, because these claims only require that the RAGE-LBE is at least 118 amino acids and is 95% identical to residues 1-118 of SEQ ID NO: 7. As set forth above, the Morser et al. patent discloses fusion proteins comprising RAGE-LBE(s), including a polypeptide that is at least 118 amino acids and is at least 95% identical (i.e. 99.7% identical) to amino acid residues 1 through 118 of SEQ ID NO: 7 (see attached sequence alignment B).

Therefore as set froth herein and previously, the combination of the prior art references of record is deemed proper, and the rejection is maintained.

Conclusion

Claims 1, 8-31 and 42-44 are rejected.

Claims 3-7 and 88-92 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

THIS ACTION IS MADE FINAL. Applicants are reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Advisory Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Gregory S. Emch whose telephone number is (571) 272-8149. The examiner can normally be reached 9:00 am - 5:30 pm EST (M-F).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeffrey J. Stucker can be reached at (571) 272-0911. The fax phone number for the organization where this application or proceeding is assigned is (571) 273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/G.E./

Gregory S. Emch, Ph.D.
Patent Examiner
Art Unit 1649
03 November 2008

/Elizabeth C. Kemmerer/
Primary Examiner, Art Unit 1646